Nutritional and Inflammatory Measures Predict Survival of Patients with Stage IV Colorectal Cancer

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Abstract

Background: The present study aimed to evaluate the prognostic impact of nutritional and inflammatory measures (controlling nutritional status (CONUT) score, prognostic nutritional index (PNI) and modified Glasgow prognostic score (mGPS)) on overall survival (OS) in patients with stage IV colorectal cancer (CRC).

Methods: Subjects were 996 patients with stage IV CRC who were referred to the National Cancer Center Hospital between 2001 and 2015. We retrospectively investigated correlations between OS and CONUT score, PNI, and mGPS. Multivariate analyses were performed using Cox proportional hazards regression models.

Results: After adjusting for known factors (age, gender, ECOG performance status, location of primary tumor, CEA levels, histological type, M category, and prior surgical treatment), all three measures were found to be independent prognostic factors for OS in patients with stage IV CRC (CONUT score, p<0.001; PNI, p<0.001; mGPS, p<0.001). Significant differences in OS were found between low CONUT score (0/1) (n=614; 61%) and intermediate CONUT score (2/3) (n=276; 28%) (hazard ratio (HR)=1.20, p=0.031), and intermediate CONUT score and high CONUT score (≥4) (n=106; 11%) (HR=1.30, p=0.044). For mGPS, significant differences in OS were found between mGPS=0 (n=633; 64%) and mGPS=1 (n=234; 23%) (HR=1.83, p<0.001), but not between mGPS=1 and mGPS=2 (n=129; 13%) (HR=1.13, p=0.319). Patients with low PNI (<48.0) (n=443; 44%) showed a significantly lower OS rate than those with high PNI (≥48.0) (n=553; 56%) (HR=1.33, p<0.001).

Conclusions: CONUT score, PNI, and mGPS were found to be independent prognostic factors for OS in patients with stage IV CRC, suggesting that nutritional and inflammatory status is a useful host-related prognostic indicator in stage IV CRC.

Trial registration: retrospectively registered

Background

The tumor-node-metastasis (TNM) eighth edition introduces a new structure, referred to as the 'prognostic factors grid,' which consists of prognostic factors for survival in various cancers (1). Although the anatomical extent of disease as categorized by TNM is a very powerful prognostic indicator in cancer, 'host-related (patient profile)' factors are also considered to have a significant impact on survival. Reportedly, modified Glasgow prognostic score (mGPS) and neutrophil-to-lymphocyte ratio are both host-related prognostic factors of pancreatic cancer, and 'nutritional status' is a host-related prognostic factor of esophageal cancer (1). Thus, nutritional and inflammatory status has gained attention from the perspective of prognosis in various malignancies (2–4). On the other hand, only 'age' and 'race,' but not nutritional and inflammatory status, are included in the host-related prognostic factors of colorectal cancer (CRC) according to the 'prognostic factors grid' (1).

mGPS and prognostic nutritional index (PNI) are representative measures of nutritional and inflammatory status. mGPS is calculated from serum albumin and C-reactive protein (CRP) (5), and PNI is calculated from serum albumin and total peripheral lymphocyte count (6). Both measures have been reported to be associated with survival in various malignancies including CRC (5–9). In addition to these two measures, controlling nutritional status (CONUT) score is recently gaining attention as a tool to evaluate the general condition of patients with cancer from nutritional and immunological perspectives (10–12). CONUT score was originally developed as an easily calculable score to replace Subjective Global Assessment and Full Nutritional Assessment, i.e., screening tools used for the early detection of undernutrition (13). CONUT score is calculated from serum albumin, total peripheral lymphocyte count, and total cholesterol. According to previous studies, CONUT score is a potential prognostic factor for survival in patients with stage I/II/III CRC and metastatic CRC receiving chemotherapy (14–17). However, prognostic factors for stage IV CRC, which includes curative resected stage IV CRC, have not been adequately examined yet.

In order to determine the optimal treatment strategy for stage IV CRC from the perspective of host status, it is of interest to evaluate whether nutritional and inflammatory measures are prognostic factors for stage IV CRC including curative resected stage IV CRC and metastatic CRC. Accordingly, the present study aimed to evaluate the prognostic impact of three nutritional and inflammatory measures (mGPS, PNI, and CONUT score) on overall survival (OS) in patients with stage IV CRC.

Methods
Study population

Subjects were consecutive patients who were initially diagnosed with stage IV CRC, and who were referred to the Department of Colorectal Surgery or Department of Gastrointestinal Oncology at the National Cancer Center Hospital between January 2001 and December 2015. Eligible patients were required to have stage IV CRC with histologically confirmed adenocarcinoma. Other histological types were excluded. Also excluded were patients with anal cancer or appendiceal cancer, and those with missing data. Initial treatment was determined at multidisciplinary team conferences held by colorectal surgeons, medical oncologists, hepatobiliary surgeons, respiratory surgeons, pathologists, radiologists, and nurses. This retrospective study was approved by the Institutional Review Board (IRB) of the National Cancer Center Hospital (IRB code: 2015–320).

Data collection

The following parameters were obtained from medical records: age, treatment year, gender, ECOG performance status, location of primary tumor (right-sided: the cecum, ascending colon, hepatic flexure, and transverse colon; left-sided: the splenic flexure, descending colon, sigmoid, rectosigmoid junction, and rectum), histological type ('differentiated,' defined as tubular adenocarcinoma and papillary adenocarcinoma; 'others,' defined as poorly differentiated adenocarcinoma, mucinous adenocarcinoma, and signet-ring cell carcinoma), and pretreatment serum carcinoembryonic antigen (CEA) levels. The M category

was assessed according to the Union for International Cancer Control TNM classification (eighth edition), which was recently revised to include the following three subcategories: M1a (metastasis confined to one organ), M1b (metastasis to more than one organ), and M1c (metastasis to the peritoneum with or without other organ involvement) (1). As for the curability of surgical treatment, subjects were classified into the following two groups: patients who received curative resection of both primary tumor and metastatic lesions, and patients who received no curative resection including those who received palliative resection of primary tumor.

Blood samples were obtained at the time of first visit or before initial treatment. CONUT scores were calculated using serum albumin, total peripheral lymphocyte count, and total cholesterol based on a previous report (13). Albumin concentrations ≥ 3.5, 3.0-3.49, 2.5–2.99, and < 2.5 g/dL were scored as 0, 2, 4, and 6 points, respectively; total lymphocyte counts ≥ 1600, 1200–1599, 800–1199, and < 800/mm^3 were scored as 0, 1, 2, and 3 points, respectively; and total cholesterol concentrations ≥ 180, 140–179, 100–139, and < 100 mg/ dL were scored as 0, 1, 2, and 3 points, respectively. Patients were divided into three groups according to CONUT scores: low (0/1), intermediate (2/3), and high (≥ 4) groups. PNI was calculated as 10 × albumin concentration (g/dl) + 0.005 × total lymphocyte count (/mm^3) (6). mGPS was scored as follows: score 0, CRP ≤ 1.0 mg/dL; score 1, CRP > 1.0 mg/dL and albumin ≥ 3.5 g/dL; and score 2, CRP > 1.0 mg/dL and albumin < 3.5 g/dL (5).

Treatment and Follow-up

For follow-up after curative resection, serum tumor marker measurements were performed every one to three months, and computed tomography (CT) scans were performed every three to six months, with a cut-off date of July 2019, as described previously(18, 19). According to Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2016 (20), postoperative chemotherapy after curative resection was not usually performed. Patients with initially unresectable stage IV CRC underwent systemic chemotherapy (multiple cytotoxic agent therapy with or without molecular targeted agents) continuously with or without palliative resection of primary tumor.

Statistical analysis

Pearson's chi-square test was used for categorical variables, and the Wilcoxon rank-sum test was used for continuous variables. OS was defined as the interval between the date of stage IV CRC diagnosis and the date of all-cause death. Survival rates were calculated by the Kaplan-Meier method, and survival curves were compared with the log-rank test. Survivors were censored as of the date of data cut-off (July 2019). Multivariate analyses were performed using Cox proportional hazards regression models to evaluate the prognostic impact of each factor on OS. The following known factors were included: age (1), gender, ECOG performance status, location of primary tumor(21), CEA levels (18), histological type, M category (19), and surgical treatment, as well as CONUT score, PNI, and mGPS, given the overlap in elements constituting each measure.

Data are expressed as numbers of patients, ratios (%), or hazard ratios (HRs) and 95% confidence intervals (CIs), as indicated. Differences with a P-value < 0.05 were considered statistically significant. All analyses were performed using JMP14 software (SAS Institute Japan Ltd., Tokyo, Japan).

Results

Study population
Between January 2001 and December 2015, a total of 1030 patients initially diagnosed with stage IV CRC were identified. Of these, patients with missing laboratory data (n = 16), patients with histologic diagnoses other than adenocarcinoma (e.g., neuroendocrine tumor) (n = 5), and patients with appendiceal cancer (n = 9) or anal canal cancer (n = 4) were excluded. Therefore, the study cohort consisted of 996 patients with stage IV CRC (Fig. 1). Follow-up was conducted for the entire cohort, with a median follow-up time of 53 months (range, 1-228 months) among survivors.

Patient characteristics
Relationships between clinicopathological characteristics and CONUT score, PNI, and mGPS are summarized in Table 1. Among the 996 CRC patients included in this study, 573 (58%) were male and 423 (42%) were female, with a median age of 61.0 years (range, 20–91 years). Almost two thirds of patients were categorized into the low-CONUT group (0/1), whereas 28% and 11% were categorized into the intermediate-CONUT group (2/3) and high-CONUT group (≥ 4), respectively. The median preoperative PNI was 48.5 (range, 24.5–68.0). According to receiver operating characteristic (ROC) curve analysis of death within 2 years after diagnosis, 48.0 was set as the cut-off value (sensitivity: 57.3%, specificity: 64.7%). Statistical analyses revealed significant associations between high CONUT scores and worse ECOG performance status (PS2, PS3, PS4) (p < 0.001), right-sided primary tumor (p = 0.004), high CEA levels (≥ 30 ng/ml) (p < 0.001), and low rate of curative resection (p < 0.001). Significant associations were also observed between low PNI and older age (≥ 65 years) (p < 0.001), female (p = 0.041), worse ECOG performance status (p = 0.001), right-sided primary tumor (p < 0.001), high CEA levels (p < 0.001), and low rate of curative resection (p < 0.001), and between mGPS = 2 and worse ECOG performance status (p < 0.001), right-sided primary tumor (p = 0.035), high CEA levels (p < 0.001), low rate of M1a (p < 0.001), and low rate of curative resection (p < 0.001).

Survival
OS curves according to CONUT score, PNI, and mGPS are provided in Figs. 2A-2C. Median survival time was 30.3 months in the low-CONUT group, 23.3 months in the intermediate-CONUT group, and 16.6 months in the high-CONUT group, with 3-year OS rates of 44.5%, 35.6%, and 24.3%, respectively, and 5-year OS rates of 27.3%, 19.8%, and 16.3%, respectively (p < 0.001). Higher CONUT scores were significantly associated with worse prognoses (Fig. 2A).

Median survival time was 33.8 months in the high-PNI group and 19.8 months in the low-PNI group, with 3-year OS rates of 48.1% and 29.5%, respectively, and 5-year OS rates of 29.0% and 17.8%, respectively (p < 0.001). The low-PNI group showed a significantly shorter OS than the high-PNI group (p < 0.001) (Fig. 2B).

Median survival time was 37.3 months in the mGPS = 0 group, 16.1 months in the mGPS = 1 group, and 14.7 months in the mGPS = 2 group, with 3-year OS rates of 51.7%, 19.3%, and 17.3%, respectively, and 5-year OS rates of 31.0%, 12.7%, and 10.2%, respectively (p < 0.001). OS was significantly shorter in mGPS = 2 and mGPS = 1 groups compared to the mGPS = 0 group (p < 0.001) (Fig. 2C).

Clinical factors affecting prognosis

In univariate analysis, CONUT score (p < 0.001), PNI (p < 0.001), and mGPS (p < 0.001) were associated with prognosis, gender (p = 0.028), ECOG performance status (p < 0.001), CEA levels (p < 0.001), histological type (p < 0.001), M category (p < 0.001), and surgical treatment (p < 0.001).

Subgroup analyses were performed by dividing the patients into those who underwent curative resection (n = 302) and those who underwent palliative resection of primary tumor / no resection (n = 694). Kaplan-Meier survival curves comparing OS between the two subgroups according to the three nutritional and inflammatory measures are shown in Figs. 3A-3F. OS curves for both subgroups showed similar trends to the overall results (Curative resection: CONUT score, p = 0.024; PNI, p = 0.073; mGPS, p = 0.064; Palliative resection of primary tumor / no resection: CONUT score, p = 0.012; PNI, p < 0.001; mGPS, p < 0.001).

Multivariate analyses were performed, adjusting for clinical factors that were significant in univariate analyses (gender, ECOG performance status, CEA levels, histological type, M category, and surgical treatment); 'age' was also included given the prior knowledge according to TNM eighth edition(1). All three measures were found to be independent prognostic factors for OS in patients with stage IV CRC (CONUT score, p < 0.001; PNI, p < 0.001; mGPS, p < 0.001). Significant differences in OS were found between the low-CONUT group and intermediate-CONUT group (HR = 1.20, 95% CI: 1.02−1.41, p = 0.031), low-CONUT group and high-CONUT group (HR = 1.57, 95% CI: 1.23−1.97, p < 0.001), and intermediate-CONUT group and high-CONUT group (HR = 1.30, 95% CI: 1.01−1.67, p = 0.044). In contrast, for mGPS, significant differences in OS were found between mGPS = 0 and mGPS = 1 groups (HR = 1.83, 95% CI: 1.53−2.18, p < 0.001) and mGPS = 0 and mGPS = 2 groups (HR = 2.07, 95% CI: 1.66−2.55, p < 0.001), but not between mGPS = 1 and mGPS = 2 groups (HR = 1.13, 95% CI: 0.89−1.42, p = 0.319). For PNI, the low-PNI group had a significantly lower OS rate than the high-PNI group (HR = 1.33, 95% CI: 1.13−1.56, p < 0.001) (Table 2).

Discussion

In the present study, we focused on stage IV CRC including curative resected stage IV CRC and unresectable metastatic CRC, and demonstrated that CONUT score, PNI, and mGPS are independent prognostic factors for OS in patients with stage IV CRC regardless of curative potential. Our results are compatible with previous reports that PNI, mGPS, and CONUT score were prognostic factors in CRC patients undergoing curative resection (5, 7, 8, 14, 17), and that CONUT score was a prognostic factor in metastatic CRC patients undergoing chemotherapy (16). To our knowledge, this is the largest study to date that comprehensively assessed the prognostic significance of nutritional and inflammatory measures in patients with stage IV CRC. Given that nutritional and/or inflammatory status has been recognized as a host-related prognostic factor in pancreatic cancer and esophageal cancer (1), nutritional and inflammatory measures may also be useful for stage IV CRC in daily clinical practice.

We demonstrated that three nutritional and inflammatory measures tended to stratify OS in subgroup analysis according to the treatment strategy. Furthermore, multivariate analyses adjusted for known factors including surgical treatment revealed that the three nutritional and inflammatory measures were all independent prognostic factors for OS in patients with stage IV CRC. These results suggest that nutritional and inflammatory status may be a useful prognostic indicator regardless of treatment strategies. It is acceptable because nutritional status affects tolerability not only surgery but also chemotherapy(2, 22−27). Patients with advanced cancer are prone to malnutrition, which in turn can lead to postoperative complications and worse postoperative survival(22, 25, 27). Malnutrition is also associated with severe chemotherapy-related toxicity and reduced survival (2, 24). Although treatment strategies for stage IV CRC vary depending on guidelines (20, 28, 29), nutritional scores can be applied to the entire population of stage IV CRC patients.

In the present study, all nutritional and inflammatory measures were evaluated based on pretreatment data and adjusted for known factors. CONUT scores range from 0−12 points, and patients are typically allocated into two to four groups based on score (14, 30). Cut-off values differ by study, with no consensus. We divided our patients into three groups (low (0/1), intermediate (2/3), and high (≥ 4), determined using pretreatment data), and found that pretreatment CONUT score was an independent prognostic factor for OS in patients with stage IV CRC. However, it remains unclear whether CONUT scores change during clinical progression of the disease. Moreover, the impact of nutritional intervention on CONUT score is unclear. A number of studies have shown that nutritional intervention improves clinical outcomes of surgery and chemotherapy (31−35), suggesting that nutritional intervention should be considered for malnourished patients. CONUT score, which comprehensively evaluates prognosis and nutritional status, can be used as a tool to screen for patients who require nutritional intervention. Further prospective studies to assess how nutritional intervention improves CONUT scores and prognosis are warranted.

Many nutritional and inflammatory measures have been reported to be associated with cancer prognosis. However, it remains controversial as to which one of those measures is the most useful. Several studies have compared CONUT score with other measures. For instance, Toyokawa et al. (11) reported that CONUT score was an independent predictor of OS and relapse-free survival among thoracic esophageal squamous cell carcinoma patients and was superior to platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, and GPS. Liu et al. (12) reported that CONUT score was an independent prognostic factor in patients with stage II-III gastric cancer receiving curative resection and adjuvant chemotherapy. In the low PNI group, CONUT score effectively stratified cancer-specific survival, suggesting it is potentially a better predictor for evaluating nutritional risk than PNI. In the present study, CONUT score, PNI, and mGPS were adjusted for known factors (i.e., age, gender, ECOG performance status, location of primary tumor, CEA levels, histological type, M category, and surgical treatment), and all three measures were independent prognostic factors in patients with stage IV CRC. Among them, however, CONUT score was significantly associated with OS. In contrast, there was no significant difference in OS between consecutive mGPS scores, suggesting that the distribution of CONUT scores was more balanced than that of mGPS scores. Unlike CONUT score and mGPS, there were only two groups by PNI; thus, CONUT scores may be more useful in stratifying patients with stage IV CRC compared to PNI and mGPS.

This study has some limitations. First, given the retrospective design and collection of data from one institution, there may have been selection bias. Second, although consecutive patients were enrolled, there have been significant changes during the long study period (2001 to 2015) in treatment strategies, such as chemotherapy. Thus, our study may not be fully reflective of current medical practice. The correlation between nutritional and inflammatory status and prognosis in stage IV CRC warrants further consideration and validation in prospective studies.

Conclusions

CONUT score, PNI, and mGPS were all independent prognostic factors for OS in patients with stage IV CRC, suggesting that nutritional and inflammatory status is a useful host-related prognostic indicator in stage IV CRC. Regardless of the TNM stage, the use of nutritional and inflammatory measures should be considered in daily clinical practice to assess host status.

Abbreviations

CEA
carcinoembryonic antigen, CONUT:controlling nutritional status, mGPS:modified Glasgow prognostic score, OS:overall survival, PNI:prognostic nutritional index, TNM:tumor-node-metastasis

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Institutional Review Board (IRB) of the National Cancer Center Hospital (IRB code: 2015–320). It was determined to be a retrospective analysis of de-identified data, and was determined to be exempt from requiring written informed consent.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YT contributed to the conception and design, data collection, analysis and interpretation, manuscript drafting. DS conceived, designed the study, performed analysis, and were responsible for writing the paper and for its supervision. NB contributed to the data collection, interpretation of data, and edited the manuscript. YN, YA, TY, TT, AT and YK contributed to the data collection, literature review, result discussion, and edited the manuscript. All authors read and approved the final manuscript. All authors have read and approved the final manuscript.

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Tables

TABLE 1. Relationships between clinicopathological characteristics and CONUT score, PNI, and mGPS.

	CONUT score					PNI			mGPS	
	All cases	Low	Intermediate	High	P value	Low	High	P value	0	
Cases	996	614 (61%)	276 (28%)	106 (11%)		443 (44%)	553 (56%)		633 (64%)	234 (23%)
Age (years)										
<65	625 (63%)	399 (65%)	170 (62%)	56 (53%)	0.052	249 (56%)	376 (68%)	<0.001	392 (62%)	
≥65	371 (37%)	215 (35%)	106 (38%)	50 (47%)		194 (44%)	177 (32%)		241 (38%)	74 (32%)
Gender										
Male	573 (58%)	340 (55%)	167 (61%)	66 (62%)	0.208	239 (54%)	334 (60%)	0.041	277 (44%)	
Female	423 (42%)	274 (45%)	109 (39%)	40 (38%)		204 (46%)	219 (40%)		356 (56%)	141 (60%)
ECOG performance status										
PS0, PS1	961 (96%)	600 (98%)	267 (97%)	94 (89%)	<0.001	418 (94%)	543 (98%)	0.001	623 (98%)	
PS2, PS3, PS4	35 (4%)	14 (2%)	9 (3%)	12 (11%)		25 (6%)	10 (2%)	10 (2%)	11 (5%)	
Location of primary tumor										
Right-sided	293 (29%)	158 (26%)	95 (34%)	40 (38%)	0.004	163 (37%)	130 (24%)	<0.001	169 (27%)	
Left-sided	703 (71%)	456 (74%)	181 (66%)	66 (62%)		280 (63%)	423 (76%)		464 (73%)	157 (67%)
CEA										
<30 ng/ml	524 (53%)	351 (57%)	133 (48%)	40 (38%)	<0.001	186 (42%)	338 (61%)	<0.001	404 (64%)	
≥30 ng/ml	472 (47%)	263 (43%)	143 (52%)	66 (62%)		257 (58%)	215 (39%)		229 (36%)	148 (63%)
Histological type										
Differentiated	897 (90%)	553 (90%)	249 (90%)	95 (90%)	0.985	396 (89%)	501 (91%)	0.527	576 (91%)	
Others	99 (10%)	61 (10%)	27 (10%)	11 (10%)		47 (11%)	52 (9%)		57 (9%)	29 (12%)
M category										
M1a	553 (56%)	355 (58%)	145 (53%)	53 (50%)	0.268	230 (52%)	323 (58%)	0.080	388 (61%)	
M1b	227 (23%)	132 (21%)	64 (23%)	31 (29%)		114 (26%)	113 (20%)		119 (19%)	64 (27%)
M1c	216 (22%)	127 (21%)	67 (24%)	22 (21%)		99 (22%)	117 (21%)		126 (20%)	64 (27%)
Surgical treatment										
Curative resection	302 (30%)	208 (34%)	74 (27%)	20 (19%)	<0.001	101 (23%)	201 (36%)	<0.001	257 (40%)	
Palliative resection of primary tumor	303 (30%) 694 (70%)	208 (34%) 406 (66%)	74 (27%) 202 (73%)	21 (20%) 86 (81%)		120 (27%) 342 (77%)	183 (33%) 352 (64%)		207 (33%) 376 (60%)	68 (29%)
No resection	391 (40%)	198 (32%)	128 (46%)	65 (61%)		222 (50%)	169 (31%)		169 (27%)	133 (57%)

CONUT: controlling nutritional status, PNI: prognostic nutritional index, mGPS: modified Glasgow prognostic score
ECOG PS: Eastern Cooperative Oncology Group performance status, CEA: carcinoembryonic antigen

TABLE 2. Univariate and Multivariate Analyses for OS

Variable	Category	Control	Univariate HR (95 % CI)	Univariate p value	Multivariate[a] HR (95 % CI)	Multivariate[a] p value
CONUT score	Intermediate	Low	1.27 (1.08-1.49)	0.004	1.20 (1.02-1.41)	0.031
High	Low		1.84 (1.45-2.31)	<0.001	1.57 (1.23-1.97)	<0.001
High	Intermediate		1.45 (1.13-1.86)	0.005	1.30 (1.01-1.67)	0.044
PNI	Low	High	1.62 (1.40-1.87)	<0.001	1.33 (1.13-1.56)	<0.001
mGPS	1	0	2.26 (1.90-2.67)	<0.001	1.83 (1.53-2.18)	<0.001
2	0		2.83 (2.28-3.47)	<0.001	2.07 (1.66-2.55)	<0.001
	2	1	1.25 (0.99-1.58)	0.063	1.13 (0.89-1.42)	0.319

[a] Adjusted for the following variables: age, gender, ECOG performance status, location of primary tumor,

CEA levels, histological type, M category, and surgical treatment.

Data are presented as hazard ratios and 95% confidence intervals.

HR: hazard ratio, CI: confidence interval, CONUT: controlling nutritional status

PNI: prognostic nutritional index, mGPS: modified Glasgow prognostic score
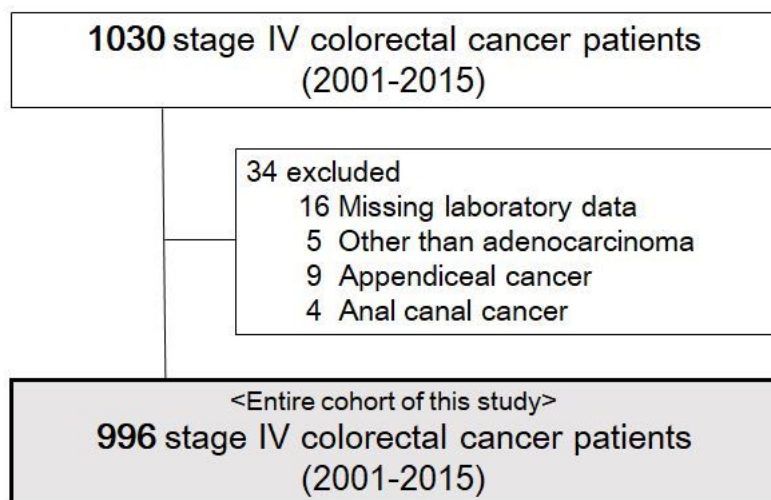
Figures

Figure 1

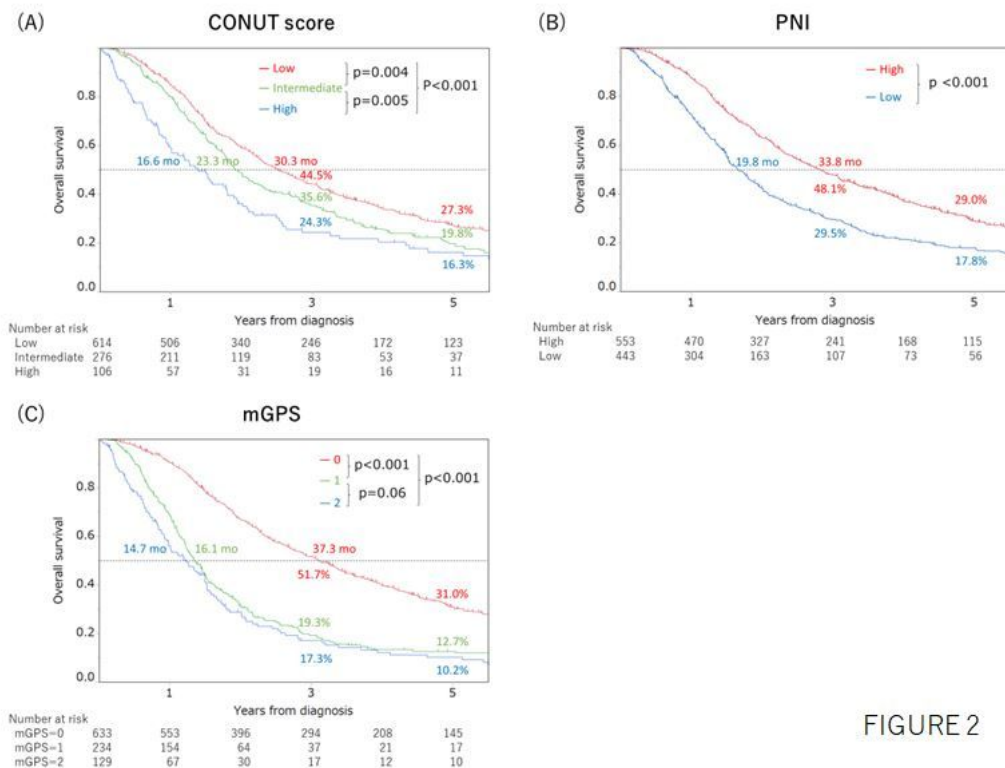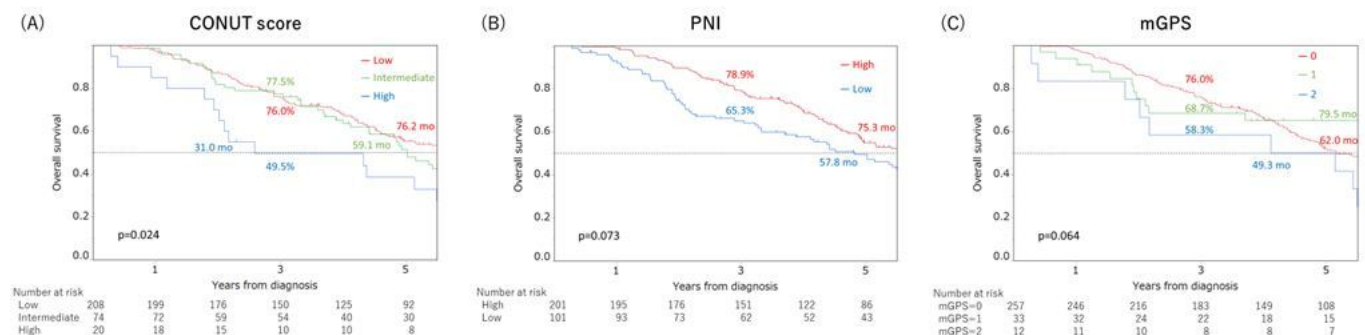Patient flow diagram. The final study cohort consisted of 996 patients with stage IV colorectal cancer.

FIGURE 2

Figure 2

a. Relationship between CONUT score and OS of patients with stage IV colorectal cancer (P<0.001). Patients were divided into three groups according to CONUT score: low (0/1), intermediate (2/3), and high (4 or higher) groups. b. Relationship between PNI and OS of patients with stage IV colorectal cancer (P<0.001). According to receiver operating characteristic (ROC) curve analysis, we set 48.0 as the cut-off value (sensitivity: 57.3%, specificity: 64.7%). c. Relationship between mGPS and OS of patients with stage IV colorectal cancer (P<0.001).
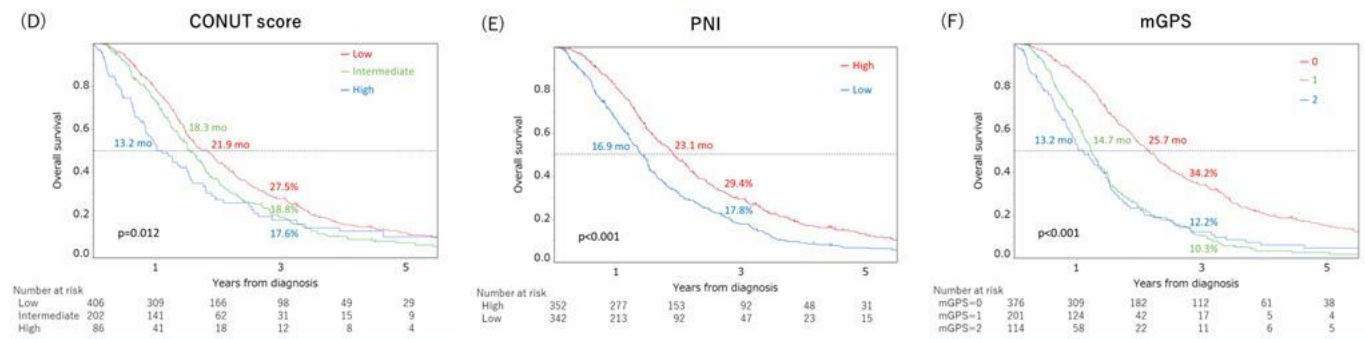

Figure 3

a-c. Relationships between three nutritional and inflammatory measures (a: CONUT score, p=0.024, b: PNI, p=0.073, c: mGPS, p=0.064) and OS of patients with stage IV colorectal cancer who received curative resection (n=302). d-f. Relationships between three nutritional and inflammatory measures (d: CONUT

score, p=0.012, e: PNI, p<0.001, f: mGPS, p<0.001) and OS of patients with stage IV colorectal cancer who received palliative resection of primary tumor or no resection (n=694).